Bayer

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3141 '01 DEC 26 P12:33

December 21, 2001

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. 00D-1538, Draft Guidance for Industry: 21 CFR Part 11; Electronic Records; Electronic Signatures Validation

Bayer Corporation appreciates the opportunity to provide comments on the Draft Guidance for Industry: 21 CFR Part 11; Electronic Records; Electronic Signatures Validation. As a manufacturer of pharmaceuticals, biologicals, medical devices, animal health products, and consumer care products, 21 CFR Part 11 Electronic Records and Electronic Signatures has a significant impact on the Bayer Corporation organization. The comments included as an attachment to this letter represent the current thinking of subject matter experts within Bayer Corporation.

In general, we felt that the guidance document did not advance the state of knowledge related to validation or compliance with Part 11 and may, in fact, add more uncertainty and confusion to the process. Computer system validation is well understood and supported by a significant number of already existing regulatory and industry source documents. Guidance is needed on how to identify systems or system components that fall under the umbrella of Part 11 requirements and how to comply with Part 11 requirements.

While perhaps beyond the immediate scope of this guidance document under review, it is critical for the industry to obtain a single standard for electronic signatures. For example, the EU, as well as several states (e.g., Massachusetts) have adopted or are currently considering implementation of requirements for electronic signatures. FDA regulations should preempt the field and thereby provide protection from disparate requirements for electronic signatures.

If you have any questions regarding our comments, please contact me.

Sincerely,

Elizabeth Gaipa

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Corporate Compliance Manager
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Attachment: Bayer Corporation Comments Guidance for Industry: 21 CFR Part 11; Electronic Records; Electronic Signatures Validation

Bayer Corporation Comments
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Page Number of PDF Guidance Document	Section Title/Description	Comment/Recommendation for Revision
General	Terminology	Recommend replacing pronouns such as "we" with "the agency" or other terminology more appropriate for a guidance document.
Page 2	2.1 Applicability	The guidance should apply to the validation of electronic systems and not records and signatures.
Page 3	4 Regulatory Requirements; What Does Part 11 Require?	To just restate that persons are required to "employ procedures and controls" does not extend to improved guidance. We encourage the agency to provide examples of the types of procedures and controls that are expected by the agency.
Page 4	5 Key Principles	This section seems to be a scaled down version of the life cycle process for computer systems. This could be misleading. It is important to see consistency from one guidance document to the next. We recommend referencing the life cycle process for computer systems including the specific requirements for Part 11.
Page 4	5.1 System Requirements Specifications	The examples in this section appear to be too high level to be of value. Recommend adding specific examples of user requirements.
Page 4	5.1 System Requirements Specifications	It may not be feasible to show traceability between the user requirements and the design specifications. Some requirements involve the system environment and are not necessarily traceable to the system requirements of the software itself. This problem worsens as the complexity and integration of systems increases.
Page 5	5.1 System Requirements Specifications Third Bullet Point	Equipment suppliers provide information on the appropriate operating environment including temperature/humidity conditions. Individuals responsible for equipment should assure that equipment is operating within recommended operating conditions. Validation should not be carried out at the extremes of the environmental operating conditions.

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Part 6	5.2 Documentation of Validation Activity	The statement, "We consider thorough documentation to be extremely important to the success of your validation effort," should be removed. This statement does not provide qualitative guidance and is more narrative in nature. We recommend that only statements that present the minimum requirements for documentation to assure compliance with Part 11 be included.
Page 6	5.2.1 Validation Plan	Clarification is needed as to how the Validation Plan differs from a traditional validation protocol. Is this section describing a Validation Master Plan?
Page 6	5.2.2 Validation Procedures	Clarification is needed. Does the term "Validation Procedures" actually mean validation protocol? If so, we recommend that the standard industry term of validation protocol be used in place of "Validation Procedures." The term "Validation Procedures" may be construed to mean standard operating procedures.
Page 6	5.2.1 Validation Plan 5.2.2 Validation Procedures 5.2.3 Validation Report	These sections require review and approval by designated management. Use of the term "management" could be interpreted as only individuals at a management level; thus unnecessarily restricting whom could review and approve the referenced documents. Recommend that the term "management" be changed to "qualified personnel."
Page 6	5.2.2 Validation Procedures	In the second sentence we recommend that the words "or reference" be added. The system configuration information could be included in another document. The revised sentence would read, "It should describe or reference the computer system configuration, as well as test methods and objective acceptance criteria, including expected outcomes."

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Page 6	5.2.3 Validation Report	It is too cumbersome to include "detailed results of the validation effort, including test results" in the validation report. This information is included in detail as part of the executed functional test protocol. Additionally, it is more efficient for the test protocol to be reviewed immediately after its execution. The completed functional test protocol is critically reviewed by a subject matter expert, where the validation report is a document that verifies that activities listed in the test protocol were executed, and approved, if necessary. We suggest that the validation report summarize the results of all testing (static, functional, dynamic) and refer to the completed functional test protocol along with other documents covering static and dynamic testing, for the detailed results.
Page 6	5.2.3 Validation Report	Recommend that the second sentence be deleted. The sentence reads, "Whenever possible, test results should be expressed in quantified terms rather than stated as "pass/fail." This information is redundant with information presented in Section 5.4.3 "How test results should be expressed."
Page 7	5.3 Equipment Installation	We question whether one can ever know whether or not software is properly installed. One really only seems to know whether or not software works after the installation is complete.
Page 7	5.4 Dynamic Testing	References to risk assessment should be included in this section.
Page 7	5.4.1 Key Testing Considerations Third Bullet Point	Clarification is needed as to whether or not live user-site testing performed under actual operating conditions allows for use of the system while the validation is ongoing. For computer systems integrated with equipment, this section implies that it is okay to use the equipment for normal production use before validation is completed.
Page 8	5.4.2 Software testing shou'd include:	The statement, "Software testing should include," should be revised to read, "Software testing may include but is not limited to…"

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Page 8	5.4.2 Software testing should include:	Program build testing should occur before structural or functional testing. Suggest that the order of the bullet points be changed to place program build testing as the first bullet point, followed by structural testing and functional testing.
Page 8	5.4.2 Software testing should include:	Structural testing also known as white box testing is a good practice. As mentioned later in the document structural testing is not always possible in the case of commercial off the shelf software, Internet applications, and routing. Structural testing may also not be absolutely necessary to achieve the intended purpose of validation of the software if the functional testing or black box testing is sufficiently conducted to cover all the scenarios. Finally, structural testing can be very costly and may not add sufficient value for certain applications.
Page 8	5.4.2 Software testing should include:	Software developers should include information as to the quality standards that were followed during software design.
Page 9	5.5 Static Verification Techniques	References to risk assessment should also be included in this section.
Page 10	5.7 Independence of Review	The term "where possible" is used in the second sentence. A guidance document provides additional framework for meeting compliance goals and the term "where possible" states there is a choice to do what is suggested. This can be misleading. We recommend that the term "where appropriate" be used instead of "where possible." In definition from the agency, when a requirement is qualified by "where appropriate," it is deemed to be "appropriate" unless documentation can justify otherwise. This ensures that rationale is provided when choices are made to use other than what is suggested in the guidance, especially if the agency will hold persons accountable for items deemed "where possible."
Page 10	5.7 Independence of Review	Engaging the services of a third party validation provider should afford a company at minimum a rebuttable presumption of proper and appropriate system validation. This is critical when there is a perceived risk to product safety or quality involved.

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Page 12	6.1.1 End User Requirements Specifications	The probability is very low that commercial software developers will provide customers with a copy of the developer's requirements specifications for comparison. This information is considered proprietary.
Page 12	6.1.1 End User Requirements Specifications	The word "all" should be removed from the last sentence of the section, "End users should be able to validate off-the-shelf software by performing "all" of the following." The scope of the work performed should be determined by the application.
Page 12	6.1.2 Software Structural Integrity	The word "all" should be removed from the first sentence. The scope of the work performed when review of the source code is not possible should be determined by the application.
Page 12	6.1.2 Software Structural Integrity Second Bullet Point	Software developers should include information as to the quality standards that were followed during software design.
Page 12	6.1.2 Software Structural Integrity	Recommend that the word "reliable" be removed in reference to a vendor audit of the software developer. The term "reliable" may be interpreted to mean that the agency would determine reliability of vendor audits during agency inspections. Internal audits are typically not available to the agency unless by special circumstances.
Page 13	6.1.3 Functional Testing of Software	Recommend that a statement be included indicating that the end user must do extensive testing of the intended functions since the end user is usually not qualified or able to fully review and test source code.
Page 13	6.1.3 Functional Testing of Software	The statement, "Note, however, we do not believe that functional testing alone is sufficient to establish software adequacy," should be deleted. If detailed functional testing is not sufficient to establish software adequacy, then the functional testing is not adequate. If the software does not meet the true minimum user requirements then it is inadequate no matter how well designed. If software is purchased from a rebuttable provider, then functional testing should be adequate.

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Page 14	6.2 The Internet	This section of the guidance document is not sufficiently developed to provide meaningful guidance. In lieu of specific guidance, we submit that industry should be permitted to rely on state-of-the-art electronic signature and encryption technology as available, with clear limitations on liability under such circumstances.
Page 14	6.2.1 Internet Validation	Recommend changing title to *Validation of Internet Usage* since the first sentence states, "We recognize that the Internet…cannot be validated…"
Page 14	6.2.1 Internet Validation	The statement, "We recognize that the Internet, as a computer system, cannot be validated because its configuration is dynamic," presents concerns related to validation. There may be limited verification and validation activities that can be performed, but cannot be validated does not seem technically correct. We recommend that the statement be revised to read, "We recognize that the Internet, as a computer system, presents unique challenges for verification and validation because its configuration is dynamic. The extent of validation may be hindered, but sufficient verification and validation can take place in due diligence." Then, a recommendation can be provided that represents "due diligence" for compliance with Part 11 from the agency's perspective.
Page 14	6.2.1 Internet Validation	This section may be interpreted to imply that one should validate the confidentiality of transmissions via the Internet. This may not be possible. One could only validate levels of security.
Page 14	6.2.1 Internet Validation	Would virtual private networks be included within the scope of this section?
Page 14	6.2.1 Internet Validation	Delivery acknowledgements using separate confirmation executed apart from the Internet (e.g., via fax or voice telephone lines) are not feasible and would eliminate some of the benefit gained by using the Internet.